

Packaging material: flask with ground-glass stopper, glass container with twist-off closure, glass container lined with polyethylene foil.

Evaluation: statistics and reaction kinetics are applied in evaluating the results.

Assessment of observed decomposition products, whether they may be formed under accelerated and long-term testing. Establishment of degradation pathway of selected decomposition products; elucidation of their structure. Assessment of applied analytical procedures. The data and the derived stability information are summarized in a stability report, as the stability profile of the investigated drug substance. The stability report is part of CMC for CTX, IND and for registration application.

Stability information: the stability report contains the following stability information:

Stability prediction drug substance

Preliminary prediction of the retest period

Storage instructions if required

Test criteria, packaging material, assessed analytical procedure and stability test protocol for accelerated and long-term testing of registration batches

Stability predictions drug product

Orientalional prediction of the chemical stability of the drug substance in solid, semisolid, liquid dosage forms

2.3. Practical Examples

The influencing factors to be investigated are now illustrated by means of a practical example.

To start the predevelopment as soon as possible, the investigations are carried out in two steps:

Preliminary investigation

Complete investigation

2.3.1. Preliminary Investigation

The experiments are organized so that the preliminary stability profile is available within 6 weeks.

Necessary amount: about 25 g.

2.3.1.1. *Moisture*

Sample: Drug substance stored in open container for 1 week at 25°C/75% r.h

Test criteria: Appearance, mass, DTA. If the drug substance has absorbed water it is investigated further in 50 mL glass container with twist-off closure under 2.3.1.2

2.3.1.2. *Temperature, Moisture*

Sample: Drug substance with and without adsorbed water in 50 mL glass container with twist-off closure

Test criteria: Appearance, decomposition, assay, DTA at the end

Analytical procedure: Orientalional validation at the beginning

Storage temperature: 70°C